REMARKS

Claims 1-5, 7-11, 13-15, and 17-32 are pending. No amendments to the claims have been made in this response.

Applicants address the Examiner's remarks in the order presented.

Applicants wish to thank the Examiner for pointing out that canceled claim 16 was missing from the listing of claims. A full listing of claims including canceled 16 is provided with this response.

Rejection under 35 USC §102

Applicants acknowledge the withdrawal of the rejection under 35 USC§102 by the Examiner.

Rejections under 35 USC §103

The rejection of claims 1-5, 7-9, 11, 13, 17-19, 21, 22, 24, 26, 28, 30 and 31 under 35 USC §103(a) as allegedly being unpatentable over Mandell in view of Wilson was been maintained by the Examiner. Applicants respectfully traverse this rejection.

In the response submitted January 31, 2008, Applicants argued the relative uptake of ^{123}Iodine in Mandell's A375 tumor cells infected with retroviruses encoding NIS gene was 7-fold greater than for non-transduced tumor cells, whereas the present invention teaches a 10-fold greater level of ^{123}Iodine uptake in tumor cells infected with adenoviral vectors encoding NIS compared to control tumor cells. Applicants argued that adenoviral vectors encoding NIS of the claimed invention unexpectedly display increased efficacy of radiolabeled iodine accumulation in the tumor cell compared to tumor cells transfected with Mandell's retroviral

vectors encoding NIS. The Office acknowledged that Example 4 in the present specification teaches a 10-fold greater ^{123}Iodine uptake in SiHa tumor cells infected with adenoviral vectors encoding NIS compared to control tumor cells; and that Mandell teaches a 7-fold greater uptake of ^{123}Iodine in A375 tumor cells infected with retroviruses encoding NIS gene compared to non-transduced tumor cells. In response to Applicants arguments, the Examiner states that the experimental findings in Mandell and in Example 4 cannot properly be compared to arrive at the conclusion of unexpected results because Mandell and Example 4 use different cells. The Office notes that Mandell teaches ^{123}Iodine uptake in A375 human melanoma cells as well as uptake in IGROV human ovarian adenocarcinoma cells, CT26 mouse colon carcinoma cells, BNL.1 ME mouse transformed liver cells and that ^{123}Iodine uptake varies for each cell type transduced with the same retroviral vector encoding the NIS iodine transporter gene. The Examiner concludes that cell type clearly affects the ^{123}Iodine uptake. Since the instant specification discloses SiHa human cervical carcinoma, the Examiner asserts the Office's position is that in order to arrive at a conclusion that the adenoviral vector expression of NIS gene is more efficacious than the retroviral vector expression of the NIS gene, the skilled artisan would have to compare the ^{123}Iodine uptake in one type of cells transduced with the adenoviral vector encoding the NIS gene and the retroviral vector encoding the NIS gene. Without such experimental testing the skilled artisan is unable to draw a conclusion that the adenoviral vector NIS gene expression is more efficacious than the retroviral NIS gene expression.

Applicants wish to note that the observations discussed above compared each cell type to its untransduced control, *e.g.*, transduced A375 cells compared to untransduced A375 cells. Another way of comparing Mandell to the instant specification is to use the FRTL-5 cells characterized by Mandell and the instant specification as an internal control in which to normalize the data between each disclosure; thus, valid comparisons can be made between Mandell and the instant specification. In Mandell, Figure 2 discloses an iodine uptake of slightly over 225 pmoles/10^5 cells in FRTL-5 cells (Figure 2A). Using the FRTL-5 cells as an internal control, the transduced cell lines shown in Figure 1 do not even approach such levels, the best iodine uptake levels are by IGROV cells and yet even the IGROV cell uptake of iodine is a mere 150 pmoles/10^5 cells. Calculating a ratio of iodine uptake of the different transduced cell lines to the FRTL-5 cells (from Figure 1 and Figure 2 of Mandell), the retroviral vector

transduced cell types of A375, BNL, CT26 and IGROV are only able to uptake iodine to 44, 26, 35 and 66 %, respectively, of the iodine uptake levels of FRTL-5. Thus, the retroviral vector transduced cells, even though they are capable of some iodine uptake, are not capable of iodine uptake to an extent even comparable to native FRTL-5 cells. In contrast, the adenoviral vector transduced SiHa cells are capable of 400% more iodine uptake as compared to FRTL-5 cells (Figure 4 of the instant specification). Clearly, this is an unexpected and surprising result.

The Examiner contends that cell type may affect iodine uptake levels and therefore can not necessarily be imputed to the effects of adenoviral transduction of NIS compared to retroviral transduction. Firstly, Mandell shows that cell types has only marginal effect on the ability of retroviral transduction of NIS to affect iodine uptake. Of all the cell types shown by Mandell, none of the cell types transduced by retroviral transduction of NIS were able to approach the level of uptake of FRTL-5 cells. Conversely, adenoviral transduction of NIS in SiHa cells produced iodine uptake levels 400% over the iodine uptake by FRTL-5. Such a dramatic effect on iodine uptake levels can not be solely attributable to the SiHa cell because this effect is also observed in adenovirus transduction of NIS in MCF-7 cells.

Thus, the experimental results of Mandell and Example 4 of the instant specification may be compared. Mandell teaches retroviral vector expression of the NIS gene in cells results in iodine transport levels that are far less than that seen in native rat FRTL-5 cells. The instant specification teaches the surprising and unexpected result that adenoviral vector expression of the NIS gene in cells results in iodine transport levels 400 % greater than native FRTL-5 cells. Applicants respectfully request withdrawal of the rejection under 35 USC §103.

The rejection of claim 10 under 35 USC §103(a) as allegedly unpatentable over Mandell and Wilson, as above, in further view of Sauvage was maintained by the Examiner. Applicants respectfully traverse this rejection. Claim 10 is dependent from claim 9. Accordingly, claim 10 is patentable over the applied art for at least the same reasons that

claim 9 from which it ultimately depends is patentable over the applied art. Reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 14, 20, 23, 25, 27, 29 and 32 under 35 USC §103(a) as allegedly unpatentable over Mandell in view of Wilson, in further view of Hidaka was maintained by the Examiner. Applicants respectfully traverse this rejection. Deficiencies inherent in combining Mandell and Wilson are discussed above. Hidaka does not remedy the aforementioned deficiencies. Accordingly, claims 14, 20, 23, 25, 27, 29 and 32 are patentable over the applied art for at least these same reasons that claim 1 from which they ultimately depend is patentable over the applied art. Reconsideration and withdrawal of this rejection are respectfully requested.

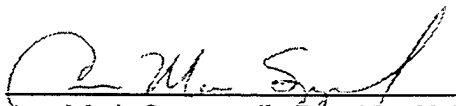
Conclusion

In view of the above amendments and remarks, Applicants respectfully request reconsideration and withdrawal of all pending rejections. Applicants respectfully submit that the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. Should the Examiner believe that anything further is desirable that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

Fees

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

Respectfully submitted,



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